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EXAMINER

BAUM, STUART F

| ART UNIT | PAPER NUMBER |
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1638

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/602,840

Applicant(s)

KIRIHARA ET AL

Examiner

Stuart Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 72,73,78,79,84,86,88-91 and 94-110 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 72,73,78,79,84,86,88-91 and 94-110 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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Objection is made to the abstract for containing more than 150 words. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc. Amending the abstract will rectify the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72-73, 78-79, 84, 86, 88-91, and 94-110 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The inventors claim a preselected DNA sequence encoding an mRNA molecule which is substantially identical, or complementary, to a mRNA encoding a plant seed storage protein, or an RNA molecule substantially complementary or substantially identical to all or a portion of a mRNA encoding a seed storage protein, encoding an RNA molecule substantially complementary or identical to all or a portion of a mRNA encoding either a 19 or 22 kD α -zein protein of SEQ ID NO's:1 (clone A20) and 2 (clone Z4), respectively. Expressing the genes in an antisense orientation in seeds reduces the endogenous amount of the amino acid leucine while increasing the endogenous amount of the amino acid lysine within the seed.

The Applicants do not explicitly state how they identified their invention, they only state "antisense expression cassettes were obtained by using sequences from cDNA clones encoding zein proteins. The cDNA clones were prepared by standard methods." The Applicants describe the sub-cloning and transformation processes whereby the clones were oriented in an antisense direction and operably linked to the Z10 and Z27 seed expressing promoters.

The Applicants do not identify structural features unique to the maize 19 and 22 kD α -zein protein, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the maize 19 and 22 kD α -zein

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proteins, it remains unclear what features identify a maize 19 and 22 kD α -zein protein, including a sequence that is substantially complementary or to all or a portion of a mRNA encoding a maize 19 and 22 kD α -zein protein, or a sequence that is substantially identical to all or a portion of a mRNA maize 19 and 22 kD α -zein protein. Since a maize 19 and 22 kD α -zein protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

Claims 72-73, 78-79, 84, 86, 88-91, and 94-110 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 72-73, 78-79, 84, 86, 88-91, and 94-110 are broadly drawn to "a plant having an increased starch content", *Zea mays* seeds "which have an increased starch extractability" and "a gene which encodes kernel hardness" comprising a DNA sequence encoding an mRNA molecule which is substantially identical, or complementary, to an mRNA encoding a plant seed storage protein, wherein the plant seed storage protein is further limited to a 19 or 22 kD α -zein protein. The specification does not teach one skilled in the art how to increase the starch content or starch extractability or kernel hardness of seeds. The specification only teaches how to make a *Zea mays* seed with a decreased amount of the amino acid leucine while increasing the amount of the amino acid lysine by transforming a *Zea mays* plant with the Z4 and A20 clones (nucleic acid sequences encoding the maize 19 and 22 kD α -zein protein, SEQ ID NO's:1 and 2, respectively) operably linked to the Z10 promoter. The Applicants present results of leucine and lysine content of seeds from transformed and non-transformed plants. It is worthwhile noting that of

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the four independent lines representing 8 samples (Table V, page 78), only three samples exhibit a statistical increase in lysine compared to the control while four of the samples exhibit a statistical decrease in leucine concentration. Therefore, less than 50% of their transformed plants actually display a desired trait using their invention.

Furthermore, Coleman et al (1997, PNAS 94:7094-7097) teach that efforts to improve protein quality of maize seeds have focused on increasing the lysine content of the protein bodies within the endosperm. Two "high-lysine" mutants were identified, opaque2 (o2) and floury2 (fl2) which have a higher lysine content due to a reduction in the α -zein protein content of the endosperm. However, this reduction in α -zein protein content is concomitant with an inferior endosperm quality (page 7094, left column, 2nd paragraph). Therefore, based on Coleman et al, reducing the α -zein protein content of maize seeds using the strategy of the Applicants, will not increase the starch content or starch extractability of maize seeds.

In addition, Marks et al (1985, J. Biological Chemistry 260(30) :16451-16459) teach there are many isoforms of the 19 and 22 kD α -zein proteins which are the result of an evolution from a common ancestor (page 16451, left column, 2nd paragraph). Marks et al divided the 22 kD α -zeins into three groups based on sequence homologies that differed by about 10% and divided the 19 kD α -zeins into five groups that differed in sequence homology by 5-25% (abstract, Figures 2 and 5, and Discussion, 1st paragraph) and these amino acid substitution/insertions/deletion and large internal duplications will intuitively affect the nutritional characteristics of the protein. Marks et al also teach that "many of these genes contain two functional polyadenylation signals and several of the genes appear to have multiple transcriptional start sites" (page 16451, left column, 2nd paragraph) and that the polyadenylation

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signals may have variable utilities. Taken together, these results suggest that there are a number of different isoforms of the 19 and 22 kD α -zein storage proteins and that they may have divergent functions.

Therefore, given the unpredictability of producing a maize seed with an increased starch content and extractability and kernel hardness using one of the many 19 and 22 kD α -zein genes in antisense orientation; given the lack of working examples of producing a maize seed with increased starch content or increase starch extractability or kernel hardness using any of the different 19 or 22 kD α -zein isoforms, given the lack of guidance in the specification for producing and identifying maize seeds with the claimed phenotypes and lack of guidance for choosing one sequence out of the multitudes of gene sequences that fall under a preselected DNA sequence encoding a RNA molecule which is substantially identical or complementary to a mRNA encoding a plant seed storage protein or substantially identical or substantially complementary to a mRNA encoding a 19 or 22 kD α -zein protein; it would require undue experimentation by one skilled in the art to practice the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 78, 79, 101, and 102 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 78, 79, 101, and 102 are drawn to a seed of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be

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transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed progeny (seeds), it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy, Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of the claims to recite that the seeds comprise the construct that was introduced into the parent seed would overcome the rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 88-89, 90-91, and 102-107 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 88-89, 90-91, and 102-107 are indefinite in their recitation "substantially complementary to all or a portion" and "substantially identical to all or a portion". The statement is vague and unclear and does not specify to what portion or percent of the sequence the Applicant is referring. The applicant could be referring to as little as one base pair.

The claims are deemed free of the prior art of record, given that the prior art does not teach or suggest transgenic *Zea mays* with decreased seed storage protein and increased starch.

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015.

Stuart Baum Ph.D.

February 5, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800

Elizabeth F. McElwain